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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/328,296	06/08/99	SIEGALL C	9632-005

HM22/1018

PENNIE & EDMONDS
1155 AVENUE OF THE AMERICAS
NEW YORK NY 10036-2711

EXAMINER	
CANELLA,K	
ART UNIT	**PAPER NUMBER**
1642	9

DATE MAILED: 10/18/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
09/328,296	Siegall et al
Examiner	**Group Art Unit**
Karen Canella	1642

☐ Responsive to communication(s) filed on _____

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3 months* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claim

☒ Claim(s) *1-37* is/are pending in the applicat

Of the above, claim(s) *10-20, 26-33, 35, and 37* is/are withdrawn from consideration

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *1-9, 21-25, 34, and 36* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☒ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☒ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

— SEE OFFICE ACTION ON THE FOLLOWING PAGES —

DETAILED ACTION

1. Please note that the examiner to which your application has been assigned at the PTO has changed.

2. Acknowledgment is made of applicants election with traverse of Group I, claims 1-9, and 34, drawn to antibodies and antibody fragments, in Paper No.8. After further review and reconsideration, the restriction will be as follows:

Group I, claims 1-9, 21-25, 34 and 36 as drawn to antibodies, antibody fragments and pharmaceutical compositions thereof, classified in class 424, subclass 130.1.

Group II, claims 10-20, drawn to nucleic acids, host cells and production of recombinant protein classified in class 536, subclasses 23.1, 23.53, and class 435, subclasses 69.1, 320.1.

Group III, claims 26, 27, 32, 33 and 37, drawn to a method for the treatment or prevention of cancer comprising the administration of antibodies or antibody fragments, classified in class 530, subclass 387.1. Claims 32, 33 and 37 will be examined with this group to the extent that they read on a method of cancer treatment;

Group IV, claims 28, 29, 30, 31, 32, 33 and 37, drawn to a method for the treatment or prevention of an immune disorder and a method for augmenting or activating an immune response comprising the administration of antibody or antibody fragments classified in class 530, subclass 387.1. Claims 32, 33 and 37 will be examined with this group to the extent that they read on a method of for the treatment or prevention of an immune disorder and a method for augmenting or activating an immune response.

Group V, claim 35, drawn to transgenic animals, classified in class 800, subclasses 8, 10, 13 and 295.

The inventions are distinct, each from the other because of the following reasons:

Inventions of Groups I, II and V are structurally and functionally different products which are made by different methods and have different uses. The examination of all groups would

require different searches in the U.S. Patent Shoes and the scientific literature and would require the consideration of different patentability issues.

The methods of Groups III and IV differ in the method objectives, method steps and parameters used to achieve efficacy.

Inventions I and III are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the antibody or antibody fragment of Invention I can be used in an in vitro diagnostic assay.

Inventions I and IV are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the antibody or antibody fragment of Invention I can be used in an in vitro diagnostic assay.

3. The traversal is on the grounds that to search all the claims of the instant invention would not place an undue search burden on the examiner. This is not found persuasive. The methods of Inventions III and IV differ in the method objectives, method steps and parameters used to achieve efficacy. Inventions I and III are related as product and process of use. Inventions I and IV are related as product and process of use. The product of the inventions can be shown to be distinct from the method of use if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the product of Invention I can also be used in methods differing

from both the methods of Groups III and IV. The products of Groups I, II and V are classified differently, necessitating different searches in the U.S. Patent shoes. Further, classification of subject matter is merely one indication of the burdensome nature of the search involved. The literature search, particularly relevant in this art, is not co-extensive and is much more important in evaluating the burden of search. Clearly different searches and issues are involved in the examination of each group.

For these reasons the restriction requirement is deemed to be proper and is adhered to. The requirement is therefore made FINAL.

4. Claims 1-37 are pending. Claims 10-20, 26-33 and 37, drawn to non-elected inventions, are withdrawn from consideration. Claims 1-9, 21-25, 34 and 36 are examined on the merits.

Specification

5. The disclosure is objected to because of the following informalities: on page ii, line 19 and page 58, line 21 it is stated "DEPOSIT OF MICROORGANISM", in reference to the deposit of the hybridoma producing the monoclonal antibody S2C6. A hybridoma is a fusion of two animal cells, not a microorganism. Appropriate correction is required.

Drawings

6. The drawings are objected to becauseof the reasons set forth on the enclose PTO948 form. Correction is required.

Claim Rejections - 35 USC § 112

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claims 1-9, 21-25, 34 and 36 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1, 8, 21, 23, and 36 recite "immunospecifically binds CD40". It is unclear how binding to CD40 differs from "immunospecifically" binding to CD40. For purpose of examination the claims will be read as binding to CD40. In addition "CD40" could refer to the CD40 antigen on B cells, soluble CD40 protein, or the CD40 ligand on T-cells. For purpose of examination, CD40 will be interpreted to read on CD40 antigen on B cells.

Claim 8 recites "95% identity". Without reference to the specific algorithm used to calculate the percent identity, the metes and bounds of the claim cannot be determined.

Claims 1, 6, 8, 9, 21, 22, 23, and 24 recite "hybridoma deposited with the ATCC and assigned the accession number PTA-110". Applicant's referral to this deposit of PTA-110 on page 58 of the specification is insufficient assurance that all of the conditions of 37 CRF sections 1.801 through 1.809 have been met. If the deposit was made under the provisions of the Budapest Treaty, filing of an affidavit or declaration by applicant, assignees or a statement by an attorney of record over his or her signature and registration number stating that the deposit has been accepted by an International Depository Authority under the provisions of the Budapest Treaty, that all restrictions upon public access to the deposits will be irrevocably removed upon grant of a patent on this application and that the deposit will be replaced if viable samples cannot be dispensed by the depository is required. This requirement is necessary when a deposit is made under the provision of the Budapest Treaty as the Treaty leaves these specific matters to the discretion of each State.

9. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to

make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

10. Claims 9, 21-25 and 36 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the monoclonal antibody S2C6 and fragments thereof, does not reasonably provide enablement for a protein comprising one or more substitutions or insertions in the primary amino acid sequence relative to that of the monoclonal antibody S2C6, or a protein that has at least 95% identity to SEQ ID NO:2 or SEQ ID NO:7 said protein having the ability to increase the binding of CD40 ligand to CD40 antigen by at least 45%. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. The specification discloses the amino acid sequence of the light chain variable domain of the S2C6 monoclonal antibody (SEQ ID NO:2) and SEQ ID NO: 3, 4 and 5 which are the corresponding CDR protein sequences. The specification discloses the heavy chain variable domain of the S2C6 monoclonal antibody (SEQ ID NO:7) and SEQ ID NO: 8, 9 and 10 which are the corresponding CDR protein sequences. The specification does not disclose any variant amino acids sequences or monoclonal antibodies which comprise one or more substitutions or insertions in the primary amino acid sequence relative to that of the monoclonal antibody S2C6. The specification does not disclose a purified protein which has at least 95% identity to SEQ ID NO:2 or SEQ ID NO:7. The specification does not demonstrate that said variant antibodies or proteins increase the binding of the CD40 ligand to the CD40 receptor by any amount. Proteins are folded 3-dimensional structures the function and stability of which are directly related to a specific conformation (Mathews and Van Holde, Biochemistry, 1996, pp. 165-171). In any given protein, amino acids distant from one another in the primary sequence may be closely located in the folded, 3-dimensional structure (Mathews and Van Holde, Biochemistry, 1996, pp. 166, figure 6.1). The specific conformation of a protein results from non-covalent interactions between amino acids, beyond what is dictated by the primary amino acid sequence. Thus, the resulting consequence of any given amino acid change is dependent upon what is substituted for the

original amino acid and the three dimensional structural environment in which the given amino acid is located (Matthews, B. "Genetic and Structural Analysis of the Protein Stability Problem"). Often, when altering the amino acid sequence of a protein, a second alteration is necessary to restore the function of the protein. For example in hemoglobin a mutation of Asp to Asn at position beta 99 results in a abnormal hemoglobin. In normal hemoglobin the Asp at position beta 99 is stabilized by a Try at position alpha 42 and an Asn at position alpha 97. The normal function of the mutated hemoglobin can be restored by producing a double mutant retaining the first mutation of Asn at position 99 beta in addition to substituting a Asp for Tyr at position alpha 42 (Kim et al, PNAS, 1994). As another example of the interactions of amino acids in a 3-dimensional protein structure, Frisch et al (Biol. Chem., Hoppe-Seyler, 1994, 375:353-356) teaches that a human Vk protein of an antibody is destabilized after a substitution of Cys 23. This de-stabilization was found to be reversed by a substitution of Try for His at position 32. Frisch concluded that there was a stabilizing interaction (non-covalent interaction) between the Cys 23 and the Tyr 32 in the original antibody. Thus it can be conceived that compensatory changes throughout a primary amino acid sequence can result in a protein having the same shape and function as the original sequence. Given the lack of guidance in the specification for choosing which amino acids to exchange, either separately or in groups, and which specific amino acids can be substituted in at any specified location, one of skill in the art would not know how to make or use the instant invention of antibody variants or proteins which differ from SEQ ID NO:2 or SEQ ID NO:7.

11. Claims 1-9, 21-25, 34 and 36 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The written description in this case only sets forth SEQ ID NO:1-10 therefore the written description is not commensurate in scope with the

claims drawn to molecules comprising SEQ ID NO: 3, 4, 8, 9, or 10 which comprise one or more substitutions or insertion in the primary amino acid sequence relative to the native monoclonal antibody S2C6 or a purified protein comprising an amino acid sequence having 95% identity to SEQ ID NO:2 or 7.

Vas-Cath Inc. V. Mahurkar, 19 USPQ2d 1111, clearly states that applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the written description inquiry, whatever is now claimed. (See page 1117). The specification does not clearly allow persons of ordinary skill in the art to recognize that the applicant invented what is claimed. (See Vas-Cath at page 1116).

Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 USC 112 is severable from its enablement provision (see page 115). With the exception of the monoclonal antibody S2C6, the skilled artisan cannot envision the detailed structure of the encompassed humanized and variant antibodies and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and a reference to a potential method of isolating it. The product itself is required. See Fiers v. Revel, 25 USPQ 2d 1601 at 1606 (CAFC 1993) and Amgen Inc. V. Chugai Pharmaceutical Co. Lts., 18 USPQ2d 1016.

However, no disclosure, beyond the mere mention of these variants and is made in the specification. This is insufficient to support the generic claims as provided by the Interim Written Description Guidelines published in the June 15, 1998 Federal Register at Volume 63, Number 114, pages 32639-32645.

Therefore only SEQ ID NO:2, 7, 3, 4, 8, 9 and 10, but not the full breadth of the claims encompassing substitutions and insertions in the amino acids sequence of monoclonal antibody S2C6 meets the written description provision of 35 USC 112, first paragraph.

Claim Rejections - 35 USC § 102

12. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371© of this title before the invention thereof by the applicant for patent.

13. Claims 1, 2, 3, 7, 8, and 34 are rejected under 35 U.S.C. 102(b) as being anticipated by either Kwekkeboom et al (Immunology, 1993, Vol. 79, pp. 439-444) or Bjorck et al (Immunology, 1994, Vol. 83, pp. 430-437). The instant claims are drawn to a purified antibody, not of the IgG1 isotype, said antibody immunospecifically binds CD40 antigen on B cells, said antibody comprising SEQ ID NO: 2, 3, 4, 7, 8, 9, or 10, or SEQ ID NO: 1 and 7, in addition to one or more substitutions or insertions in the primary amino acid sequence relative to native monoclonal antibody S2C6 as secreted by the hybridoma deposited at the ATCC and assigned the accession number PTA-110, or has at least 95% identity to SEQ ID NO:2 or 7. Kwekkeboom et al disclose the purified monoclonal antibodies of the IgG2 isotype 5D12, 3C6 and 3A8 which bind the CD40 antigen on B cells. As the antibodies are not the S2C6 antibody, they must have an amino acid sequence comprise one or more substitutions or insertions in the primary amino acid sequence relative to the S2C6 antibody. Bjorck et al disclose the purified monoclonal antibody of the IgM isotype, 17:40, which binds the CD40 antigen on B cells. As 17:40 is not the S2C6 antibody, it must have an amino acid sequence which comprises one or more substitutions or insertions in the primary amino acid sequence relative to the S2C6 antibody. The amino acids sequences of 5D12, 3C6, 3A8 and 17:40 are not disclosed by either Kwekkeboom et al or Bjorck et al, so it is not possible for the examiner to determine if SEQ ID NO: 2, 3, 4, 7, 8, 9 or 10 are

present in the amino acid sequences of these prior art antibodies. It is known from the art that the CDR region of the antibody is responsible for binding to the antigen. SEQ ID NO: 3, 4, 8, 9 and 10 represent the CDR sequences of the claimed antibody which binds the CD40 antigen on B-cells. Since the prior art antibodies also bind the CD40 antigen on B cells it is possible that they possess a like CDR region, and therefore would have the amino acid sequence of SEQ ID NO: 3, 4, 8, 9 or 10 or have an amino acid sequence which is 95% identical to SEQ ID NO:2 or 7. The office does not have the facilities and resources to provide the factual evidence needed in order to establish that the product of the prior art does not possess the same material, structural and functional characteristics of the claimed product. In the absence of evidence to the contrary, the burden is on the applicant to prove that the claimed product is different from those taught by the prior art. See In re Best 562F.2d 1252, 195 USPQ 430 (CCPA 1977) and Ex parte Gray 10 USPQ 2d 1922 (PTO Bd. Pat. App. & Int. 1989).

14. Claims 1, 2, 3, 7, 8, and 34 rejected under 35 U.S.C. 102(e) as being anticipated by de Boer (USP 5,874,082). The instant claims are drawn to a purified antibody, not of the IgG1 isotype, said antibody immunospecifically binds CD40 antigen on B cells, said antibody comprising SEQ ID NO: 2, 3, 4, 7, 8, 9, or 10, or SEQ ID NO: 1 and 7, in addition to one or more substitutions or insertions in the primary amino acid sequence relative to native monoclonal antibody S2C6 as secreted by the hybridoma deposited at the ATCC and assigned the accession number PTA-110, or has at least 95% identity to SEQ ID NO:2 or 7. De Boer discloses the purified humanized monoclonal antibody 5D12 of the IgG2 subtype which bind the CD40 antigen on B cells. As the antibodies are not the S2C6 antibody, they must have an amino acid sequence comprise one or more substitutions or insertions in the primary amino acid sequence relative to the S2C6 antibody. The office does not have the facilities and resources to provide the factual evidence needed in order to establish that the product of the prior art does not possess the same SEQ ID NOs of the claimed product. In the absence of evidence to the contrary, the burden is on

the applicant to prove that the claimed product is different from those taught by the prior art. See In re Best 562F.2d 1252, 195 USPQ 430 (CCPA 1977) and Ex parte Gray 10 USPQ 2d 1922 (PTO Bd. Pat. App. & Int. 1989).

Claim Rejections - 35 USC § 103

15. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103© and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

16. Claims 1, 2, 3, 7, 8, 34, and 4 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kwekkeboom et al or Bjorck et al (supra) in light of Uckun et al (Blood, 1990, Vol. 76, pp. 2449-2456). The instant claims are drawn to a purified antibody, not of the IgG1 isotype, said antibody immunospecifically binds CD40 antigen on B cells, said antibody comprising SEQ ID NO: 2, 3, 4, 7, 8, 9, or 10, or SEQ ID NO: 1 and 7, in addition to one or more substitutions or insertions in the primary amino acid sequence relative to native monoclonal antibody S2C6 as secreted by the hybridoma deposited at the ATCC and assigned the accession number PTA-110, or has at least 95% identity to SEQ ID NO:2 or 7. Further embodiments include the monoclonal antibody which is fused to a protein which is not an antibody. Kwekkeboom et al or Bjorck et al teach a purified antibody, not of the IgG1 isotype, said antibody immunospecifically binds CD40 antigen on B cells, said antibody comprising SEQ ID NO: 2, 3, 4, 7, 8, 9, or 10, or SEQ ID NO: 1 and 7, in addition to one or more substitutions or insertions in the primary amino acid sequence relative to native monoclonal antibody S2C6 as secreted by the hybridoma deposited at the ATCC

and assigned the accession number PTA-110, or has at least 95% identity to SEQ ID NO:2 or 7. Kwekkeboom et al or Bjorck et al do not teach the fusion of monoclonal antibodies to a non-immunoglobin protein. Uckun et al teach the anti CD40 antibodies fused to non-immunoglobin proteins. It would have been *prima facia* obvious to one of ordinary skill in the art at the time the claimed invention was made to fuse the monoclonal antibodies of Kwekkeboom et al or Bjorck et al with a non-immunoglobin protein. One of ordinary skill in the art would have been motivated to do so with a reasonable expectation of success by the teachings of Uckun et al on the usefulness of anti CD40 antibodies fused to toxins for the treatment of clonogenic B-lineage leukemia and Non-Hodgkin's Lymphoblastic cells.

17. Claims , 2, 3, 7, 8, 34, 4 and 5 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kwekkeboom et al or Bjorck et al and Uckun as applied to claims 2, 3, 7, 8, 34, and 4 above, and further in view of Siegall. The instant claims are drawn to monoclonal antibodies fused to non-immunoglobin protein as taught by Kwekkeboom et al and Bjorck et al and Uckun et al. Further embodiments include bryodin as the non-immunoglobin protein. Siegall teaches bryodin fused to a monoclonal antibody that binds to a tumor associated cell surface antigen that is capable of internalization. It would have been *prima facia* obvious to one of ordinary skill in the art at the time the claimed invention was made to fuse the monoclonal antibodies as taught by Kwekkeboom et al and Bjorck et al and Uckun et al to the toxin bryodin. One of ordinary skill in the art would have been motivated to do so with a reasonable expectation of success by the teachings of Siegall on the usefulness of bryodin as a immunotoxin when fused to a monoclonal antibody which is internalized after being bound by a tumor associated antigen.

18. Claims 1, 2, 3, 7, 8, 34 and 6 are rejected under 35 U.S.C. 103(a) as being unpatentable over de Boer (USP 5,874,082) in light of what is suggested in de boer (USP 5,874,082). The instant claims are drawn to a purified antibody, not of the IgG1 isotype, said antibody

immunospecifically binds CD40 antigen on B cells, said antibody comprising SEQ ID NO: 2, 3, 4, 7, 8, 9, or 10, or SEQ ID NO: 1 and 7, in addition to one or more substitutions or insertions in the primary amino acid sequence relative to native monoclonal antibody S2C6 as secreted by the hybridoma deposited at the ATCC and assigned the accession number PTA-110, or has at least 95% identity to SEQ ID NO:2 or 7. Further embodiments include said antibody comprising the variable domain of monoclonal antibody S2C6 and a human constant region. De Boer teaches the humanized purified monoclonal antibody 5D12. De Boer does not provide experimental data on the humanization of S2C6 but suggests that "Any of the anti-CD40 monoclonal antibodies of this present invention are capable of being humanized using ...techniques as applied to monoclonal antibody 5D12". De Boer presents data on the reactivity of 5D12 in relation to S2C6 (Fig. 5A). It would have been *prima facia* obvious to one of ordinary skill in the art at the time the claimed invention was made to make the humanized version of the S2C6 monoclonal antibody. One of ordinary skill in the art would have been motivated to do so with a reasonable expectation of success by the teachings of de Boer on the desirability of obtaining a humanized antibody for treatment of humanized subjects, said antibodies providing a reduced immunogenicity in humans (column 3, lines 17-22 and column 13, lines 2-15).

19. Claims 9, 21, 22, 23, 24, 25 and 36 are free of the art.

20. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. Accession Number S69899, discloses SEQ ID NO:8 as an immunoglobin V region from IgG rheumatoid factors. Accession Number S67941 discloses SEQ ID NO:8 as the immunglobin V region of an ati-thyroidgloulin antibody. Accession number C29380 discloses SEQ ID NO:4 in the immunoglobulin V region of mouse antibodies to blood group A and B substances. Accession Number W78434 discloses SEQ ID NO:10 in the light chain of an antibody targeted to HER3 clone 18. Accession Number Y06716 discloses SEQ ID NO:10 in an antibody directed toward

the thrombopoietin receptor. USP 5,530,101 discloses SEQ ID NO:10 in the heavy chain of mouse Fd79 antibody (SEQ ID NO:48). USP 5,872,215 discloses SEQ ID NO:10 in the Vh domain of the CEA6 antibody (SEQ ID NO:18).

Conclusion

21. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Karen Canella whose telephone number is (703) 308-8362. The examiner can normally be reached on Monday through Friday from 8:30 am to 6:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa, can be reached on (703) 308-3995. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Karen A. Canella, Ph.D.

Patent Examiner, Group 1642

October 8, 2000

ANTHONY C. CAPUTA
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600